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Fibrous Tumors of Bone

Kenneth E. Marks, MD and Thomas W. Bauer, MD, PhD†*

Benign and malignant fibrous tumors of bone are some of the most common tumors and tumor-like lesions encountered by the orthopedic surgeon. This article reviews the clinical, radiographic, and histologic features of benign and malignant fibrous and fibrohistiocytic lesions that arise within bone and discusses currently accepted biopsy and treatment techniques. Fibrous tumors arising in soft tissue may secondarily erode into bone, but discussion of soft tissue lesions is beyond the scope of this article. Similarly, a wide variety of bone lesions will have fibrous areas, often secondary to hemorrhage and/or repair, but will not be discussed in detail.

Although nomenclature for this family of lesions in controversial, Table 1 lists the principal fibrous lesions according to their biologic behavior.

FIBROUS DYSPLASIA

Terminology

In 1891 von Recklinghausen[72] reported a group of benign fibro-osseous lesions of bone using the term *osteitis fibrosa*. This group of patients was probably a heterogeneous one and may have included cases that would now be classified as fibrous dysplasia. During the next several decades, osteitis fibrosa was used to describe most benign fibro-osseous lesions, including multifocal lesions that occurred in the absence of hyperparathyroidism.[34] In 1937 McCune and Bruch[51] reported a case of osteodystrophia fibrosa in which multiple fibro-osseous lesions occurred associated with precocious puberty and skin pigmentation. At about the same time, Albright and coworkers[1] reported several similar cases, and this combination of features was subsequently termed *Albright's syndrome*. Lichtenstein and Jaffe[48] recognized that the bony lesions may occur in one or more sites in the absence of the other clinical features and proposed the term *fibrous dysplasia*.

Clinical Features

The clinical spectrum of fibrous dysplasia varies from asymptomatic, monostotic lesions to extensive skeletal deformities associated with polyostotic involvement. In an encyclopedic review of fibrous dysplasia by Harris and coworkers,[31] the spectrum of clinical features is thoroughly described. In that series, 70 per cent of patients presented complaining of bone pain and 5 of 20 females presented with abnormal vaginal bleeding. Most patients had developed skeletal deformities by age 10 years, but some were essentially asymptomatic until late in life. Regression of bone lesions has rarely been documented. Patients with fibrous dysplasia appear to have a slightly increased risk for developing secondary sarcomas, usually osteosarcoma.[22,31,36]

Radiographic Features

In long bones, fibrous dysplasia is either metaphyseal or diaphyseal and may be centrally or eccentrically located. The lesions are intramedullary radiolucencies with a hazy quality usually described as a "groundglass" appearance (Fig. 1). The involved areas are well defined and frequently associated with a zone of reactive sclerosis. There may be endosteal scalloping or erosions leading to cortical thinning. Spinal lesions are also well defined, expansile, radiolucent lesions with multiple internal septations or striations.[59]

Fibrous dysplasia frequently weakens the bone, causing secondary deformities, especially in weight-bearing bones. A primary ex-

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Table 1. *Fibrous and Fibrohistiocytic Lesions*

Benign
Fibrous dysplasia
Fibrous cortical defect
Nonossifying fibroma
Benign fibrous histiocytoma
Osteofibrous dysplasia (ossifying fibroma)
Intermediate biologic behavior
Desmoplastic fibroma
Fibrous inflammatory lesions
Erdheim-Chester disease
Hand-Schüller-Christian disease
Malignant
Fibrosarcoma
Malignant fibrous histiocytoma

ample of this is the pronounced curvature of the femoral neck and proximal femur, commonly referred to as a "shepherd's crook" deformity.

Technetium-99 bone scans show intense activity over the area of fibrous dysplasia. However, because bone scans are nonspecific, they are of little or no use in the diagnosis of fibrous dysplasia or its complications. The main benefit of the computed tomography (CT) scan is the accurate assessment of the lesion's extent.

The radiographic appearance of malignant degeneration of fibrous dysplasia depends, to some extent, on the histologic type of tumor involved. Lesions that have poorly defined areas of osteolysis, cortical destructions, and soft tissue masses adjacent to the cortical disruption should suggest malignant transformation.[59]

Histology

Lesions of fibrous dysplasia are characterized by poorly oriented trabeculae of woven bone. The trabeculae tend to form "C"- or "S"-shaped profiles and characteristically lack osteoblastic rimming (Fig. 2). Small foci of cartilage may be present. The fibrous stroma consists of spindled cells with oval nuclei and indistinct cytoplasmic borders. Areas of hemorrhage may be present and are often accompanied by osteoclastic giant cells. If the lesion is complicated by a pathologic fracture, then reactive new bone, including trabeculae with prominent osteoblastic rimming, may be present along with a periosteal reaction and other features of a fracture callus. Lesions in the mandible tend to have thicker trabeculae and may demonstrate spheroidal calcifications.

Treatment

Most monostotic lesions of fibrous dysplasia are asymptomatic and need no treatment. Harris and associates[31] recognized four indications for surgical treatment: (1) severe or progressive deformity of an extremity, (2) nonunion of a fracture, (3) a femoral shaft fracture in an adult, and (4) persistent pain. Stephenson and colleagues[69] studied the results of treatment of 65 symptomatic lesions and found that the results in the lower extremity were dependent on the patient's age. In patients 18 years of age or older who were treated with either open or closed methods, the results were satisfactory in 88 per cent of cases. In contrast, patients who were under 18 years old usually had an unsatisfactory

Figure 1. Fibrous dysplasia. An adolescent girl presented with right hip pain. An anteroposterior radiograph of the pelvis shows a lesion in the right femoral neck. The lesion has a "ground-glass" appearance and is marginated by mature reactive bone, which is especially pronounced distally. There is a nondisplaced femoral neck pathologic fracture.

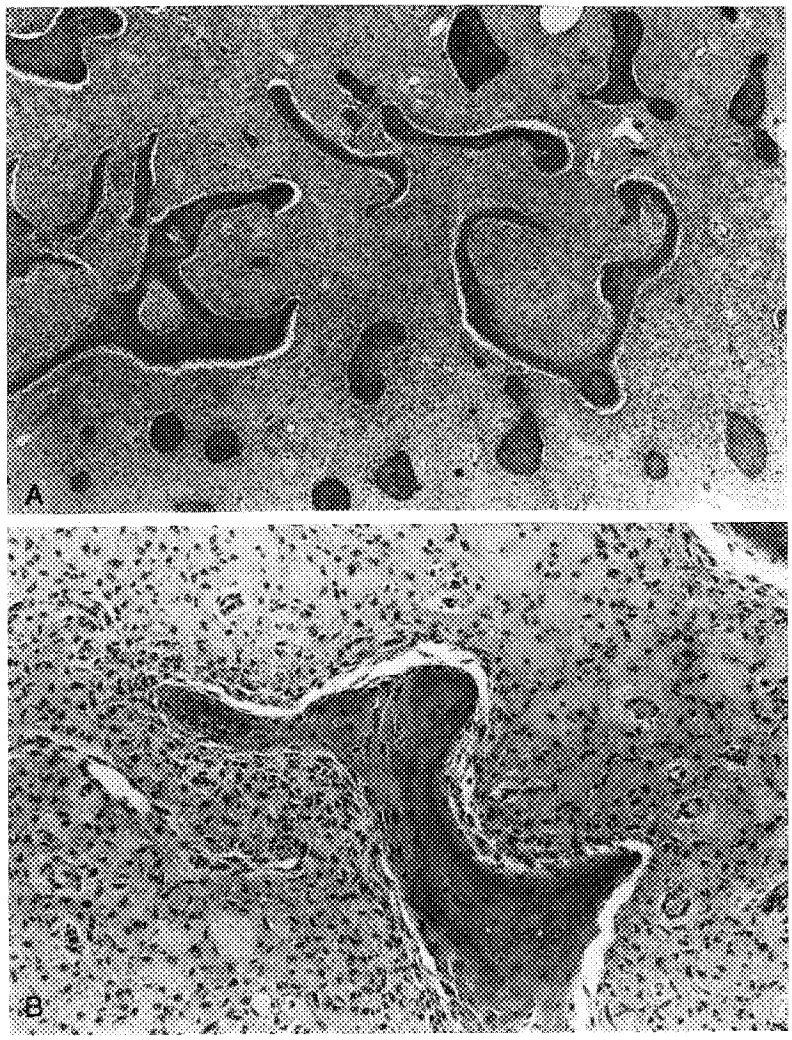

Figure 2. Photomicrograph of fibrous dysplasia. *A*, The stroma is fibrous and the trabeculae tend to form unusual shapes, often similar to the letters "C" or "S." *B*, Higher magnification photomicrograph of fibrous dysplasia. The trabeculae of woven bone tend to lack osteoblastic rimming.

outcome. In that group, 88 per cent of the lesions that were treated closed and 81 per cent of those treated with intralesional excision and autogenous cancellous bone grafting had unsatisfactory results. Eighty-six per cent of the patients treated by internal fixation had satisfactory results. Stephenson and associates concluded that internal fixation does not alter the basic disease process, but provides mechanical support of the structurally compromised bone. Freeman and coworkers[27] also observed good results in the six femora treated with multiple osteotomies to correct severe deformities along with internal fixation with a Zickle nail.

Other methods have also been proposed to provide mechanical support for dysplastic bone. Enneking and Gearen[23] treated 15 patients who had fibrous dysplasia of the femoral neck with autogenous cortical bone graft, usually from the fibula. They ultimately achieved good results in all patients, regardless of age. Allografts may be superior to autogenous cortical grafts because they are absorbed more slowly than autogenous cancellous bone grafts.

In summary, when treating symptomatic fibrous dysplasia in adults or children, internal fixation, either with intramedullary devices or cortical grafts, is superior to intralesional excision and bone grafting with autogenous cancellous bone grafts. In expendable bones a symptomatic lesion can be successfully treated with en bloc excision. Radiotherapy plays no role in the treatment of fibrous dysplasia.

FIBROUS CORTICAL DEFECT AND NONOSSIFYING FIBROMA

Terminology

In 1941, Sontag and Pyle[65] described the radiographic features of lytic ("cystic-like") lesions in the metaphysis of children. They reported the gradual disappearance of the lesions and speculated that the lesions might be composed of cartilage. In 1942, Jaffe and Lichtenstein[40] reviewed a series of tumors that had been classified as variants of giant cell tumor of bone, many of which had the radiographic features described by Sontag and Pyle.[65] Within this diverse group of lesions they recognized a benign fibrous lesion that had often been considered to be a healing xanthomatous or xanthogranulomatous variant of giant cell tumor and applied the term *nonossifying fibroma.* Several years later Hatcher[32] suggested that lesions of the type described by Jaffe and Lichtenstein might represent developmental abnormalities rather than neoplasms and proposed the term *metaphyseal fibrous defect.* Radiographic studies[10] showed that small cortical defects may be present in up to 30 to 40 per cent of children under the age of 2 years, most often in the metaphysis of the femur, and that a small proportion of these lesions enlarged and extended into the medullary cavity.

Although terminology remains controversial, it appears that a non-neoplastic fibrous proliferation occurs commonly in the metaphysis of long bones in children. This eccentric lesion is probably a developmental defect and is appropriately classified as a benign fibrous cortical defect. Many of these lesions spontaneously involute; others persist as small lytic lesions that may gradually "move" toward the diaphysis as the bone grows in length. Other lesions enlarge,[74] may involve the medullary cavity, and may be complicated by pathologic fracture. It is reasonable to use the term nonossifying fibroma for the latter lesion, recognizing that it may not represent a true neoplasm.

Clinical Features

Most fibrous cortical defects are completely asymptomatic and are incidentally detected during evaluation for another complaint. Larger lesions may be associated with a pathologic fracture.

Radiographic Features

Radiographically, nonossifying fibroma and fibrous cortical defects are very similar in appearance. Nonossifying fibromas are larger and more often symptomatic. Both lesions are found in similar or identical anatomic locations.[58] Fibrous cortical defects, however, occasionally can be found in multiple locations whereas nonossifying fibromas are less commonly multifocal. These lesions typically affect long tubular bones of the lower extremity. It is uncommon for the upper extremity to be affected, but when it is the humerus is the most typical site of involvement. Fibrous cortical defects are well-delineated, circular or oval lesions with smooth or lobulated edges (Fig. 3). The adjacent bone is typically sclerotic and the periosteal surface is nonreactive. Usually they arise in the metaphysis near the physis. As the person grows, the lesion appears to migrate toward the diaphysis, and at the same time, parts of the lytic lesion may develop sclerosis. The larger nonossifying fibromas are more elongated and multiloculated. They frequently exhibit slight bony expansion and cortical thinning (Fig. 4). Greyson and Pang[29] note that their appearance on bone scan changes during maturation. They will show mild to moderate uptake during the phase of involution or healing.

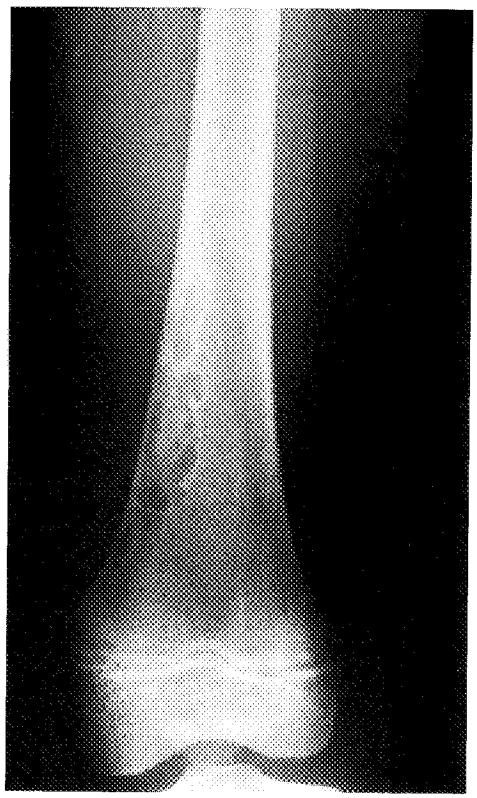

Figure 3. Fibrous cortical defect. An 8-year-old boy was asymptomatic until he sprained his knee while playing. An anteroposterior radiograph shows a large eccentric defect well marginated in the distal femur.

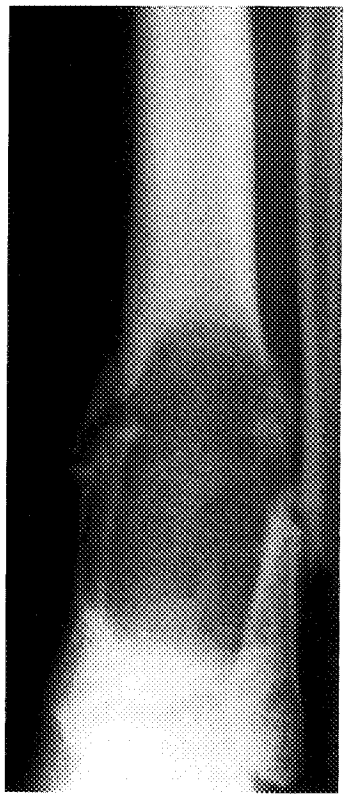

Figure 4. Nonossifying fibroma. A 17-year-old boy presented following a second pathologic fracture of his distal tibia. The anteroposterior radiograph shows a well-marginated expansile lesion of the distal tibia metaphysis.

When the lesion has healed or is inactive it is not apparent on a bone scan.

Histology

The fibrous cortical defect or nonossifying fibroma is characterized by a proliferation of benign spindled fibroblasts (Fig. 5). A suggestion of a storiform pattern may be present, but there is no nuclear pleomorphism and mitoses are very rare. If the lesion has undergone a fracture, then variable amounts of hemorrhage, hemosiderin deposition, reactive new bone formation, and osteoclastic-type giant cells may be present. Occasional cells with lipid vacuoles are also common. The original description of this lesion by Jaffe and Lichtenstein emphasized the presence of foam cells having the light microscopic appearance of histiocytes.[38–40] Since then, some electron microscopic studies have suggested that the lipid accumulates secondarily within cells of fibroblastic origin,[8,68] while others have provided evidence of histiocytic[33] or even lipoblastic[46] origin (see later discussion).

Treatment

Because these fibrous lesions are self-limiting, surgery is usually not indicated. Large nonossifying fibromas occasionally cause repeated pathologic fractures. Under these circumstances intralesional excision with or without bone graft is indicated.[24] Chemotherapy or radiation therapy plays no role in the treatment of fibrous cortical defects of nonossifying fibromas.

JAFFE–CAMPANACCI SYNDROME

In 1983 Campanacci and coworkers[11] brought attention to a syndrome of multiple nonossifying fibromas in combination with other lesions including café-au-lait spots, mental retardation, hypogonadism, and ocular or cardiovascular abnormalities usually without neurofibromas. Several similar pa-

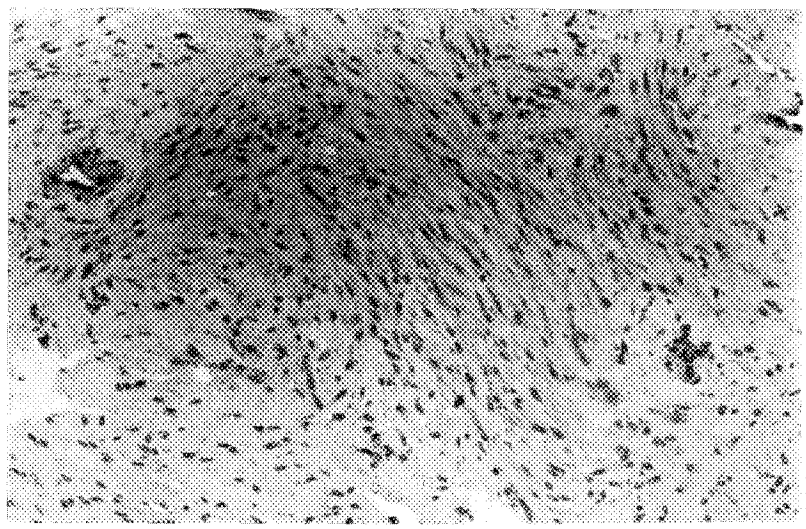

Figure 5. Photomicrograph of fibrous cortical defect. The lesion consists of fusiform cells separated by a collagen matrix. There is no nuclear atypia, and mitoses are very rare.

tients had been described briefly by Jaffe.[38] The clinical spectrum of this syndrome as well as its pathogenesis is unclear. Mandibular lesions are common[54] as are pathologic fractures through the nonossifying fibromas. Although most of the skeletal abnormalities involute, locally aggressive growth has been reported.[6]

OSSIFYING FIBROMA (OSTEOFIBROUS DYSPLASIA)

Terminology

Although not recognized as distinctive, probably the first report of this lesion was by Frangenheim in 1921,[26] who considered it congenital osteitis fibrosa. Montgomery[55] described a lesion in the mandible as "ossifying fibroma," and in 1966, Kempson[42] reported two examples of "ossifying fibroma of long bones" occurring in the tibia in infants. Additional small series of cases were reported[49,63] that attempted to define ossifying fibroma as a unique lesion separate from fibrous dysplasia and congenital pseudarthrosis of the tibia. More recently, Campanacci and Laus[11,12] reported 35 patients with a similar or identical lesion always involving the tibia, fibula, or both. These authors proposed the term *osteofibrous dysplasia* instead of ossifying fibroma. Other authors also have adopted the term osteofibrous dysplasia.[13,56]

Clinical Features

Ossifying fibromas probably occur most frequently in the mandible. In this location, they tend to occur in adults, are relatively well circumscribed, and rarely recur after curettage. Osteofibrous dysplasia of long bones, however, usually involves the tibia and/or fibula of infants or children. Most patients present with swelling, with or without pain. The lesions are usually monostotic, but both bones of the same limb can be affected. A similar or identical lesion may be associated with congenital pseudarthrosis of the tibia in some children with von Recklinghausen's neurofibromatosis.

Radiographic Features

The lesion is usually lytic and eccentrically located in the diaphysis or metaphysis. The cortex may be expanded and the bone, especially in the tibia, may be bowed in an anterior–posterior direction. The lytic areas may have a confluent, groundglass, or vacuolated appearance[13] and are rimmed by reactive bone that is more extensive than usually seen in fibrous dysplasia. The differential diagnosis based on the radiograph may include fibrous dysplasia, nonossifying fibroma, or adamantinoma. The intracortical location, however, is a helpful clue in distinguishing the lesion from fibrous dysplasia.

The isotope scan typically shows intense increase in uptake. Enneking[24] observed that angiograms showed little or no soft tissue reactive vascularity, but in growing active lesions there may be heavy vascular proliferation within the lesion.

Histologic Features

This lesion is characterized by a fibrous stroma in which trabeculae of woven bone frequently demonstrate osteoblastic rimming (Fig. 6). The orientation of the trabeculae may appear more logical than in fibrous dysplasia, but very often the histologic distinction between these two lesions is problematic; radiographic correlation is usually helpful. Adamantinoma of long bone is a tumor that may show radiographic features identical to osteofibrous dysplasia. An adamantinoma also may have large areas of fibrous spindled stroma with trabeculae of woven bone, and extensive sampling may be required to identify the epithelial component that allows recognition of an adamantinoma.

Treatment

In one of the early descriptions of the lesion, Kempson[42] recommended an extraperiosteal resection of bone and periosteum. One of the two patients in his study experienced local recurrence. Campbell and Hawk[13] reported that all four of their patients who had undergone intralesional excision experienced recurrence and Nakashima and colleagues[56] reported recurrence in all 10 cases treated by curettage. Campanacci and Laus[11,12] reported a wide range of biologic behavior but noted that most lesions cease growth when the patient reaches 15 years of age. Based on these observations, Enneking[24] has recommended conservative treatment with appropriate bracing to prevent deformity in a growing child. He advises delaying surgery for as long as practical because after the cessation of growth the lesion is less likely to recur after surgical excision. If surgery becomes necessary in a growing child, wide excision of bone is required to prevent recurrence. In an adult aggressive recurrence does not necessarily follow a marginal or even intralesional excision. Radiation therapy and chemotherapy are not indicated in the management of ossifying fibroma.

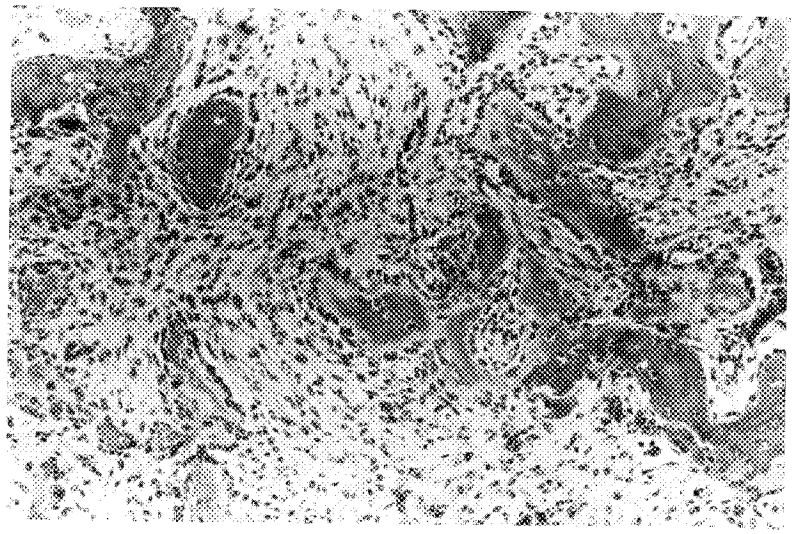

Figure 6. Photomicrograph of osteofibrous dysplasia (ossifying fibroma) of the tibia. The surfaces of the trabeculae tend to be lined with osteoblasts.

BENIGN FIBROUS HISTIOCYTOMA

The vast majority of benign fibrous lesions occur in the metaphysis of long bones as described above. Other lesions of similar histologic appearance have been identified in older patients, frequently in the pelvis.[15,17] This latter group of lesions tends to demonstrate more prominent foam cells, somewhat more variable cytoplasmic borders, and may have a more well-defined sclerotic rim. Although considered part of the spectrum of nonossifying fibromas by some authors, others classify these lesions as xanthofibromas, fibroxanthomas, or benign fibrous histiocytomas. This terminology is consistent with the currently accepted classification for soft tissue tumors. While it may not be possible to separate all nonossifying fibromas from benign fibrous histiocytomas based on histologic appearance or even fundamental cell of origin, it is probably reasonable to consider them as separate lesions based on their different radiographic and clinical presentation.

Clinical Features

While nonossifying fibromas tend to arise eccentrically in the metaphysis of a long bone, benign fibrous histiocytomas are more widespread, arising in the diaphysis or epiphysis of long bones or in the pelvis.[15,17,67] Patients may present at any age but are likely to present complaining of pain. Pain in the absence of a fracture is much more typical of a benign fibrous histiocytoma than a nonossifying fibroma.[25]

Radiographic Features

The radiographic presentation of benign fibrous histiocytoma of bone helps differentiate this lesion from a nonossifying fibroma. While nonossifying fibromas are almost always found in the metaphysis, benign fibrous histiocytomas are seen in the diaphysis as well as the metaphysis.[15] The initial lesion is centrally located whereas the fibrous cortical defect or nonossifying fibroma is usually eccentric, arising from within the cortex. As the lesion becomes larger, it may erode the endosteal surface of the cortex. The lesion itself is purely lytic with sharply defined margins and no demonstrable matrix.[15]

Histology

Benign fibrous histiocytomas are characterized by plump, foamy, histiocytic-type cells in a background of benign spindled fibroblasts (Fig. 7). Like nonossifying fibromas, a variable amount of hemorrhage and hemosiderin deposition may be present, accompanied by scattered osteoclastic giant cells. The periphery of the lesion may contain spicules of new bone, but bone formation is generally minimal. When present, osteoclasts tend to aggregate around areas of vasculature of hemorrhage rather than showing the even distribution characteristic of a giant cell tumor. Nuclear pleomorphism should be minimal, but rare mitoses may be present. Distinction from a giant cell reparative granuloma, brown tumor of hyperparathyroidism, and nonossifying fibroma may require clinical and radiographic correlation.

Treatment

The results of intralesional excision and bone grafting of benign fibrous histiocytomas have been relatively disappointing. Clark and colleagues[15] have reported that three of seven patients treated with intralesional exci-

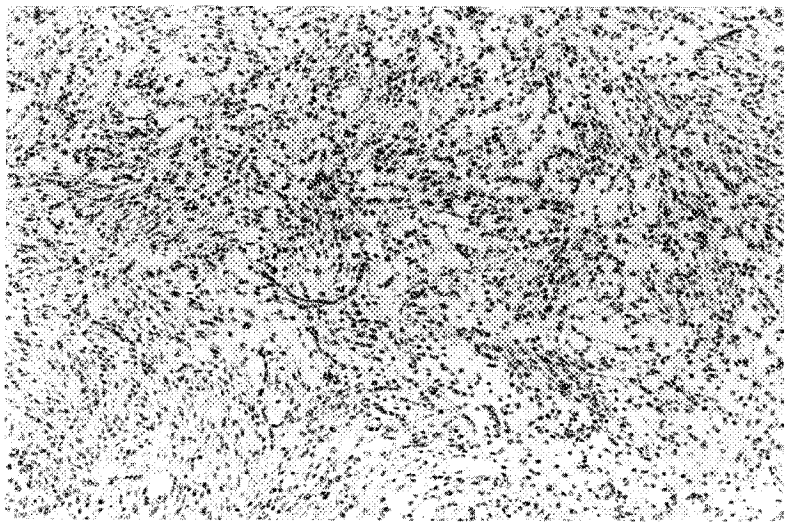

Figure 7. Photomicrograph of a benign fibrous histiocytoma of the iliac wing. The lesion contains spindled fibroblastic cells that may develop a "storiform" growth pattern. There is no nuclear atypia, however, and mitoses are rare. Foamy histiocytes may be a prominent feature, and this lesion may also be termed a fibroxanthoma or xanthofibroma of bone.

sion experienced local recurrence. The recurrence was more extensive than the original lesion and resulted in amputation in two of three patients. The one lesion that had an en bloc excision did not recur. Clark suggested wide local excision as the treatment of choice. Although no studies have confirmed the efficacy of marginal and wide excision, their use seems justified in light of a 45 per cent recurrence rate with intralesional excision. Tumors that cannot be excised en bloc without causing unacceptable functional deficits should be widely curetted and treated with adjuvant therapy such as phenol or cryotherapy. Such a treatment scheme, while logical, has not been proven experimentally. Radiation therapy and chemotherapy have no place in the treatment of benign fibrous histiocytoma of bone.

FIBROUS INFLAMMATORY LESIONS

A variety of inflammatory lesions of bone may show fibrous or fibrohistiocytic histologic patterns. These include chronic osteomyelitis, eosinophilic granuloma and related histiocytoses, storage diseases such as Gaucher's disease, and Erdheim-Chester disease. Although these lesions show histologic features similar to benign fibrous and fibrohistiocytic tumors they are frequently multifocal and show radiographic and clinical features that usually allow distinction from fibrous tumors of bone. A thorough discussion of these inflammatory lesions is beyond the scope of this article; the reader is referred to recent reviews by Groopman, Cline, and Mille and their coworkers.[16,30,52]

DESMOPLASTIC FIBROMA

Terminology

First described by Jaffe in 1958[39] the desmoplastic fibroma is a rare tumor that has been considered the bony counterpart of the desmoid tumor (aggressive fibromatosis) of soft tissue. Fewer than 100 cases have been reported and although the terminology for this lesion is well recognized, specific criteria for diagnosis are not. As with the soft tissue counterpart, the distinction between an aggressive fibromatosis and a low grade fibrosarcoma may be difficult. Although commonly considered to be of fibroblastic origin, Lagace and coworkers[44] have provided electron microscopic evidence supporting an origin from myofibroblasts.

Clinical Features

This rare tumor may develop at any age but is most common in the first three decades of life.[28] Patients usually present complaining of a mass with or without pain. The symptoms reflect a slow-growing lesion and may have been present for several years. Lesions usually arise in the metaphysis of long bones of the appendicular skeleton.

Radiographic Features

Desmoplastic fibromas are well-defined osteolytic lesions with a sclerotic margin without any evidence of calcified or ossified matrix production. They enlarge the bone diameter by the process of endosteal erosion and limited periosteal bone formation (Fig. 8). Within the lesion there is a delicate trabeculated soap bubble or honeycombed pattern. Desmoplastic fibromas most typically arise in the mandible, femur, humerus, tibia,

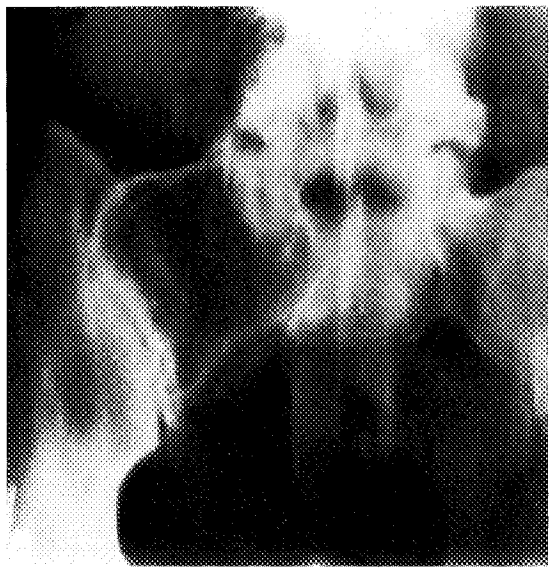

Figure 8. Desmoplastic fibroma. An adult male presented with a 1-year history of vague lower back pain. An anteroposterior radiograph and tomogram of the pelvis demonstrated a well-marginated radiolucent lesion of the right sacrum. There is enlargement of the right sacrum and no periosteal reaction.

radius, or innominate bone.[59] They are centrally located in the metaphysis and rarely cross an open physeal plate to the epiphysis. In the most common form they may resemble a nonossifying fibroma, chondromyxoid fibroma, giant cell tumor, aneurysmal bone cyst, unicameral bone cyst, or fibrous dysplasia. Desmoplastic fibromas occasionally become large and appear more aggressive, with permeative bone destruction, irregular and coarse trabeculation, cortical erosion, a soft tissue mass, and pathologic fractures. When these occur a fibrosarcoma or skeletal metastases must be added to the differential diagnosis.

Radionucleotide bone scans show increased activity confined to the area of the lesions. The margins of the lesion demonstrate more activity than the center. This finding is best seen on large lesions. CT and magnetic resonance (MR) scans are useful because they delineate the soft tissue extent of the lesion. MR images are excellent in defining the intramedullary spread of the tumor. Currently, angiography is infrequently performed for this lesion. When it is, there is little neovascular response around the lesion and scant vascularity within the tumor.[24]

Histology

The histologic features of this tumor are similar to extraskeletal fibromatoses. Sheets of spindled fibroblasts are separated by extracellular collagen fibers. Scattered osteoclastic giant cells are often present especially associated with areas of hemorrhage and new bone formation. There is minimal nuclear pleomorphism and mitoses are rare, but the distinction between desmoplastic fibroma and a low grade fibrosarcoma is indistinct. Fibrosarcomas tend to have more plump nuclei and greater cellularity with a corresponding decrease in extracellular collagen.

Treatment

The recognition of desmoplastic fibroma is important because it is more aggressive than other benign fibrous tumors. Gephardt and associates[28] reviewed the literature and found 26 patients who were treated with either curettage or bone grafts or both. Of that group, 42 per cent (11 patients) had recurrence. Of the patients in the literature who were initially treated with resection (intralesional, marginal, or wide), 4 (25 per cent) of 16 had local recurrence. In Gephardt's own series an intralesional procedure was performed as the initial treatment in six patients and four (67 per cent) had a recurrence. Two patients underwent marginal resection; neither recurred. Bertoni and colleagues[5] reported four cases treated with wide segmental resection. None had a local recurrence of the tumor.

Enneking[24] recommends wide surgical margins for the treatment of desmoplastic fibromas. Bertoni and colleagues[3] also conclude that the lesion should be excised en bloc with a continuous thin layer of healthy tissue around the tumor (wide margin). Gephardt and coworkers[28] concur that a wide or marginal resection is the procedure of choice if it can be done without causing major functional deficit. If the tumor is located about the knee, the proximal humerus, or the pelvis, and cannot be resected without major functional deficit, they recommend intralesional curettage and bone grafting. The rationale for this is that such a strategy is likely to be successful more than half of the time. Gephardt and colleagues speculate that adjuvants such as phenol may decrease the rate of local recurrence. Others have successfully used cryotherapy as an adjuvant for other aggressive benign tumors and, by analogy, it may be helpful in the treatment of desmoplastic fibroma. Recurrent tumors may be satisfactorily treated with a marginal or wide resection.

Enneking[24] speculates that radiation ther-

apy may be useful in suppressing local recurrence, but there is little reported experience with this type of treatment. He concludes that it should be considered a clinical trial and be reserved for those cases that otherwise could be controlled only by amputation. Chemotherapy plays no role in the treatment of desmoplastic fibroma.

PERIOSTEAL DESMOID

Terminology

In 1951, Kimmelstiel and Rapp[43] described a benign fibrous lesion originating beneath the periosteum and associated with erosion of the underlying bone. They referred to this lesion as a "periosteal desmoid." Although Dahlin[17] has suggested that the periosteal desmoid is a hypocellular variant of a nonossifying fibroma, most other authors suggest that it more closely resembles a fibromatosis arising in a periosteal location.[67] Since the desmoplastic fibroma of bone resembles an intraosseous fibromatosis, Schajowicz[62] classifies the periosteal desmoid as a periosteal variant of desmoplastic fibroma.

Clinical Features

The periosteal desmoid is a rare lesion that apparently shows a strong male predilection. It is most common between ages 10 and 20 years and tends to occur at the insertion of the most distal portion of the adductor tendon on the posterior medial cortex of the femur adjacent to the medial femoral condyle.

Radiographic Features

Periosteal desmoids have a characteristic radiographic appearance and location (see preceding text). They produce a saucer-like defect in the cortex with a well-demarcated reactive margin.[24] The oval-shaped lesion is associated with a periosteal response, which can be exuberant and irregular in outline. There may be a soft-tissue swelling overlying the bony defect (Fig. 9).

Plain radiographs are usually enough to make the diagnosis, but CT can be useful in equivocal or atypical cases.[57] The CT scan shows the tumor without matrix calcification and the absence of a cortical shell or reactive bone. Enneking[24] reports that isotope scans will show a focal increase in activity, which corresponds almost exactly to the size of the lesion.

Histologic Features and Treatment

Most authors regard periosteal desmoids as cellular fibrous lesions with extensive collagen, identical in appearance to desmoplastic fibroma or a soft tissue fibromatosis. Lesions of this type are satisfactorily treated by block excision, although curettage has also been successful.[67] Other authors apply a broader definition for periosteal desmoid, considering it essentially a hypocellular variant of fibrous cortical defect.[17] A lesion of this histologic appearance is benign, self-limited, and of good prognosis, requiring no surgical treatment. Mirra[53] has emphasized the distinction between periosteal desmoid and the so-called "cortical irregularity syndrome." While the former has a tendency to recur locally, the latter is self-limited, requiring no treatment. There is no indication for radiation or chemotherapy in the treatment of periosteal desmoids.

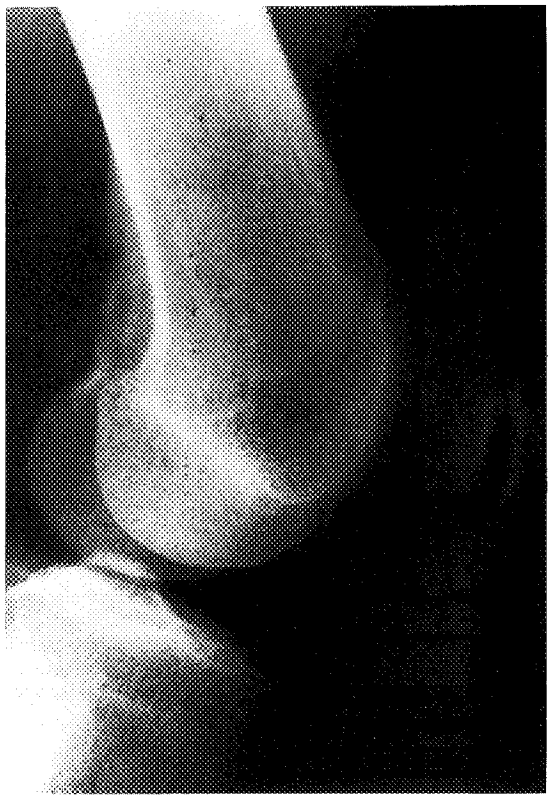

Figure 9. Periosteal desmoid. A 17-year-old boy was asymptomatic until he sprained his knee while playing football. A lateral radiograph shows a radiolucency on the posterior face of the distal metaphysis of the femur.

FIBROSARCOMA OF BONE

Terminology

Fibrosarcomas of bone are rare tumors that may arise within the medulla (central) or periosteal surface (peripheral). The distinction

between a low grade fibrosarcoma and other locally aggressive, but benign lesions (desmoplastic fibroma and periosteal desmoid) is indistinct. Similarly, the criteria for separating a high grade fibrosarcoma from a malignant fibrous histiocytoma of bone are also somewhat ill-defined (see later).

Clinical Features

Primary fibrosarcomas of bone may present at any age from birth to the elderly but may show a slight predominance in young adults. They are most common in the long bones of the lower extremity or the humerus and are rare in the axial skeleton.[5,37,45] Patients usually present complaining of pain and a mass, often complicated by a pathologic fracture. Fibrosarcomas have also been reported complicating pre-existing benign bony lesions, including Paget's disease, fibrous dysplasia, or a bone infarct. Congenital lesions, or those occurring in young children, tend to have a better prognosis than tumor in patients over 10 years of age.[18]

Radiographic Features

The radiographic abnormalities of fibrosarcomas of bone are not specific. A similar radiographic presentation may be seen with malignant fibrous histiocytoma, telangiectatic osteosarcoma, lymphoma, plasma cell myeloma, desmoplastic fibroma, and skeletal metastases. The tumor usually involves the metaphyseal or metadiaphyseal portion of long bones. Its position may be central or eccentric. Specific sites of involvement in order of decreasing frequency are the femur, tibia, humerus, fibula, radius, and ulna.[58,59] Fibrosarcomas are osteolytic with geographic motheaten or permeative patterns of bone destruction and, in general, a wide zone of transition (Fig. 10). There is little or no periosteal reaction or sclerosis of the surrounding bone. Cortical destruction and soft tissue masses are frequently seen, but visible tumor matrix is not present.

Technetium-99 bone scans show intense increased uptake over the primary lesion and adjacent bone. They are especially useful in detecting distant osseous metastases. MR scans clearly show the extent of intraosseous tumor spread and soft tissue extension.

Histology

Fibrosarcomas are characterized by interwoven bundles of spindled cells with narrow, tapering nuclei and ill-defined cytoplasmic borders. In low grade lesions there is considerable extracellular collagen, while higher grade tumors show more dense cellularity and a reduction of extracellular matrix. Tumor necrosis may be present and is a feature helpful in defining the grade of the tumor. Nuclear pleomorphism is usually not prominent in a fibrosarcoma (Fig. 11). The

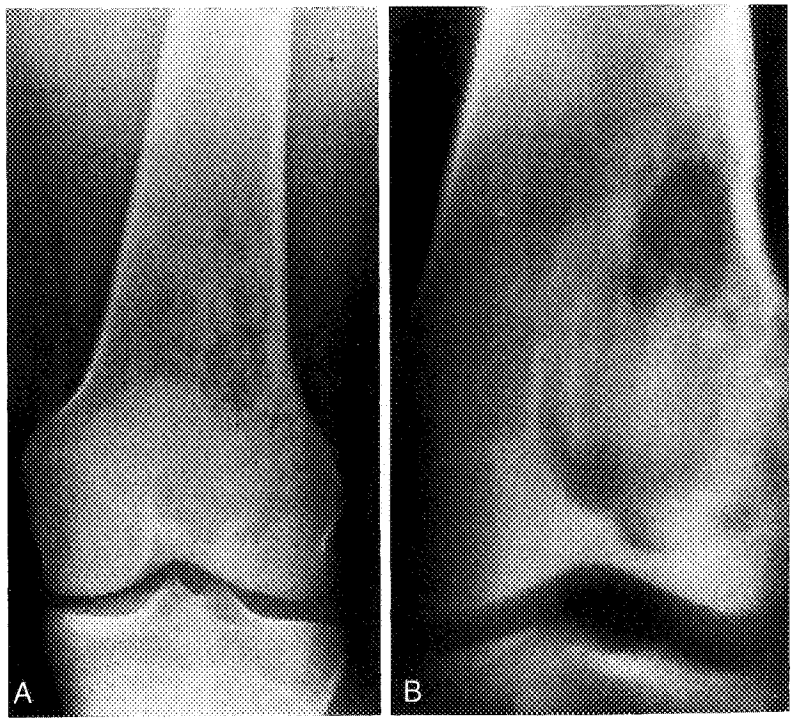

Figure 10. Fibrosarcoma of bone (stage IIA). A 37-year-old male presented with a 2-month history of increasingly severe knee pain. *(A)*, Anteroposterior radiograph shows a permeative destructive lesion involving the distal metaphysis of the femur. *(B)*, Tomogram reveals an extension of the tumor into the epiphysis.

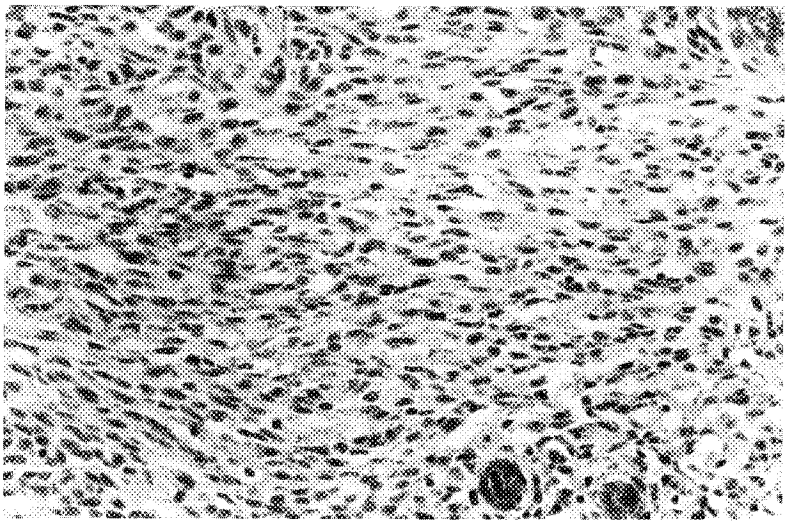

Figure 11. Photomicrograph of a fibrosarcoma of bone. This cellular tumor consists of spindled, fibroblastic cells with relatively frequent mitoses. Nuclear pleomorphism is variable, but usually not a prominent feature. The tumor illustrated in this case would be considered grade II (of III) by conventional histologic grading. Grading by the Enneking system would be difficult, but the tumor should probably be considered high grade (II of II).

distinction between a low grade fibrosarcoma and desmoplastic fibroma is problematic, and to a certain extent simply reflects a matter of grade. The presence of numerous mitoses, atypical mitoses, and an aggressive radiographic appearance should suggest a low grade malignancy. Similarly, the distinction between a high grade fibrosarcoma and a malignant fibrous histiocytoma of bone may be indistinct. Occasional pleomorphic nuclei may be seen in a high grade fibrosarcoma but are more characteristic of malignant fibrous histiocytoma. Taconis and Van Rijssel[70] have suggested that the histologic distinction between fibrosarcoma and malignant fibrous histiocytoma provides no significant prognostic information, whereas histologic grading of either is of predictive value.

Treatment

Adequate treatment requires at least wide surgical margins achieved either by en bloc resection or amputation. Enneking[24] differentiates between low grade stage I lesions and the more aggressive stage II tumors. He states that stage I lesions respond well to wide excision, whereas stage II lesions need a radical margin for local control. The need for radical margins frequently necessitates amputation.

The results of treatment have been discouraging. Taconis and Van Rijssel[70] reported a 5-year survival rate of 34 per cent. Sim and associates[64] found only 28.7 per cent of the patients survived 5 years. The local recurrence rate is similar to other malignant tumors of bone. Chemotherapy and radiation therapy thus far have not proven themselves valuable adjuncts in the treatment of fibrosarcoma of bone.

MALIGNANT FIBROUS HISTIOCYTOMA

Terminology

The term *malignant fibrous histiocytoma* was first applied in the early 1960s to soft tissue tumors in which the spindled cells interweave in a storiform pattern. Although largely fibroblastic, many of these tumors showed plump histiocytic-type cells and demonstrated features in vitro typical of histiocytes. Although recent immunohistochemical studies suggest that the tumor cells may be more closely related to fibroblasts than true histiocytes, the term *malignant fibrous histiocytoma* became rapidly accepted as a label for a pleomorphic, high grade sarcoma with little matrix production. In the early 1970s primary bone malignant fibrous histiocytomas were recognized, and numerous studies now document its clinical and pathologic features.[14,19,35,50,66]

Clinical Features

Malignant fibrous histiocytomas may arise at any age but are most common in middle-aged adults. They are slightly more common in men than women and are most frequent in the long bones of the lower extremity. They are also common in the pelvis but rare in the vertebral column or ribs. Most patients present complaining of pain.

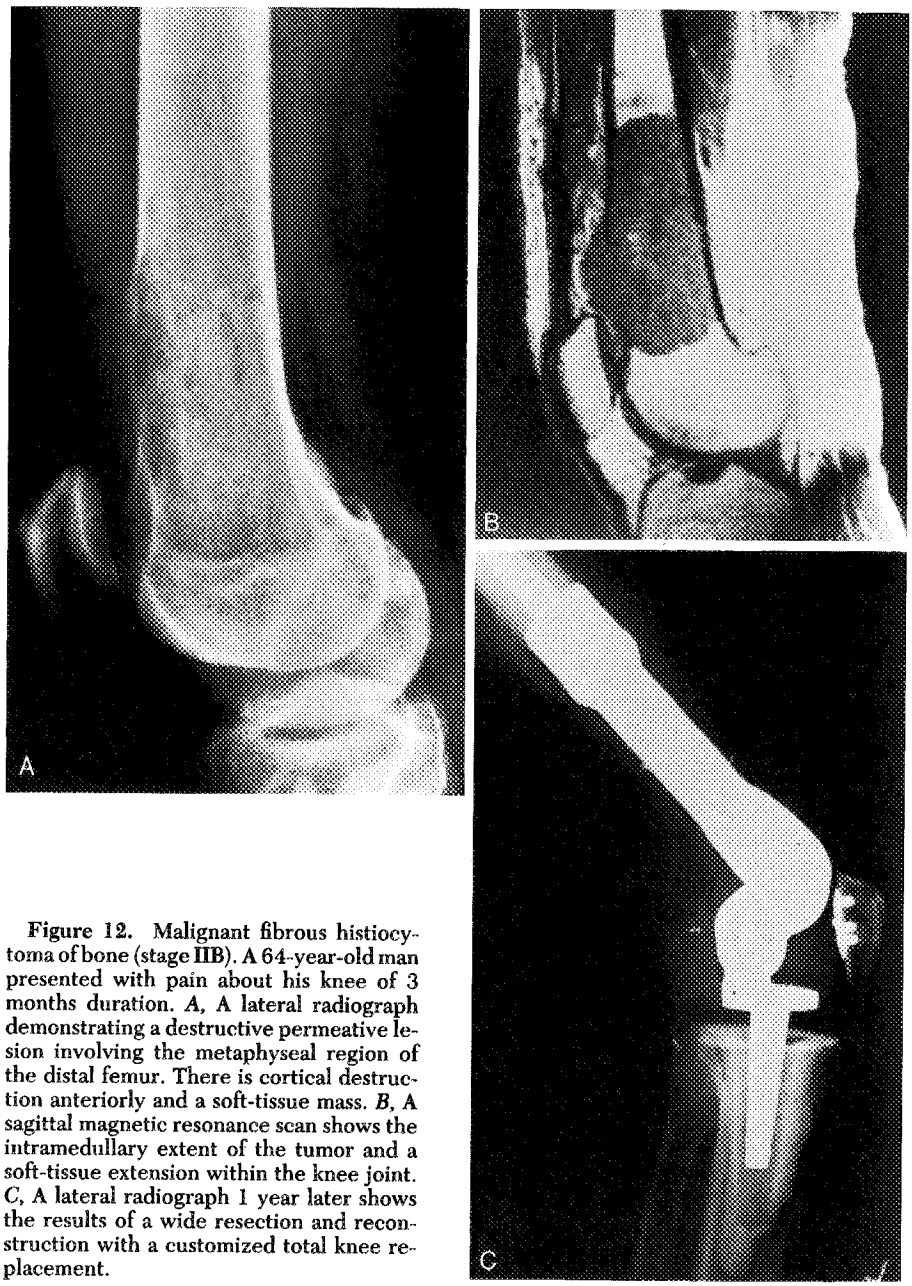

Figure 12. Malignant fibrous histiocytoma of bone (stage IIB). A 64-year-old man presented with pain about his knee of 3 months duration. *A*, A lateral radiograph demonstrating a destructive permeative lesion involving the metaphyseal region of the distal femur. There is cortical destruction anteriorly and a soft-tissue mass. *B*, A sagittal magnetic resonance scan shows the intramedullary extent of the tumor and a soft-tissue extension within the knee joint. *C*, A lateral radiograph 1 year later shows the results of a wide resection and reconstruction with a customized total knee replacement.

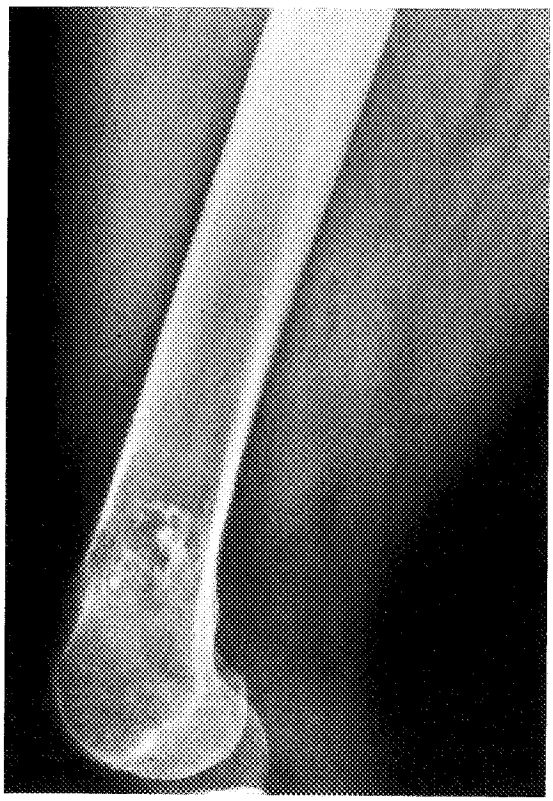

Figure 13. Malignant fibrous histiocytoma of bone. A 27-year-old man with a stage IIA lesion of the distal femur and a pre-existing bone infarction.

Radiographic Features

The radiographic features of malignant fibrous histiocytoma indicate an aggressive skeletal process but are not diagnostic of this tumor. The tumors are osteolytic with a motheaten or permeative pattern of bone destruction (Fig. 12).[7,14,35,59] They frequently cause cortical erosion and soft tissue masses but periosteal new bone formation and endosteal scalloping are uncommon.

Coexisting radiographic features of benign conditions, such as bone infarcts, fibrous dysplasia, and Paget's disease, may be present (Fig. 13). The differential diagnosis for these radiographic abnormalities includes osseous metastases, plasmacytoma, lymphoma, osteolytic osteosarcoma, fibrosarcoma, and dedifferentiated chondrosarcoma.

Technetium-99 bone scans show intense uptake in the bone far beyond the margins that are apparent on plain radiographs. Angiography demonstrates extensive neovascularity in the soft tissue around the lesion. MR images can best delineate the soft tissue mass and the intramedullary spread of the lesion. The MR image should be carefully inspected for signs of metastatic spread.

Histology

The presence of anaplastic tumor giant cells in a spindled stroma is characteristic of malignant fibrous histiocytoma (Fig. 14). The cells show striking nuclear pleomorphism and abundant cytoplasm. The mononuclear cells are usually fibroblastic and may show a cartwheel or storiform growth pattern, but this is nonspecific. Tumor necrosis is frequently present and mitoses are variable and sometimes common. There may be peripheral reactive new bone formation but the tumor itself fails to produce any matrix beyond collagen. The tumor may be quite vascular and a pattern resembling a malignant hemangiopericytoma may be focally present. As mentioned earlier, the distinction between a malignant fibrous histiocytoma and a high grade fibrosarcoma lies principally in the presence of anaplastic tumor giant cells. In some tumors the extracellular collagen may develop a lace-like pattern and closely resemble osteoid. McCarthy and colleagues[50] have stressed the importance of mineralization of this matrix in distinguishing osteosarcoma from malignant fibrous histiocytoma.

Treatment

En bloc surgical resection or amputation is the mainstay of treatment of malignant fibrous histiocytoma of bone. The results of surgery alone, however, have been disappointing. Capanna and coworkers[14] reported a 5-year survival rate of only 28 per cent for surgery alone. In contrast, 57 per cent of patients who underwent surgery and adjuvant chemotherapy survived 5 years. Following inadequate surgery, however, adjuvant chemotherapy was ineffective in reducing local recurrence or improving survival. The overall recurrence rate was 31 per cent. As expected, the incidence of local recurrence was higher after inadequate surgery (64 per cent). Wide surgical margins reduced the recurrence rate to 17 per cent for resection and 21 per cent for amputations. The lowest local recurrence rate was 6.5 per cent after radical surgical procedures.

Other authors have confirmed the positive role of chemotherapy in the treatment of malignant fibrous histiocytoma.[2,20,73] Urban and colleagues[71] reported on five patients with malignant fibrous histiocytoma of bone treated with preoperative chemotherapy, including high dose methotrexate with citrovorum rescue. One patient had a clinically

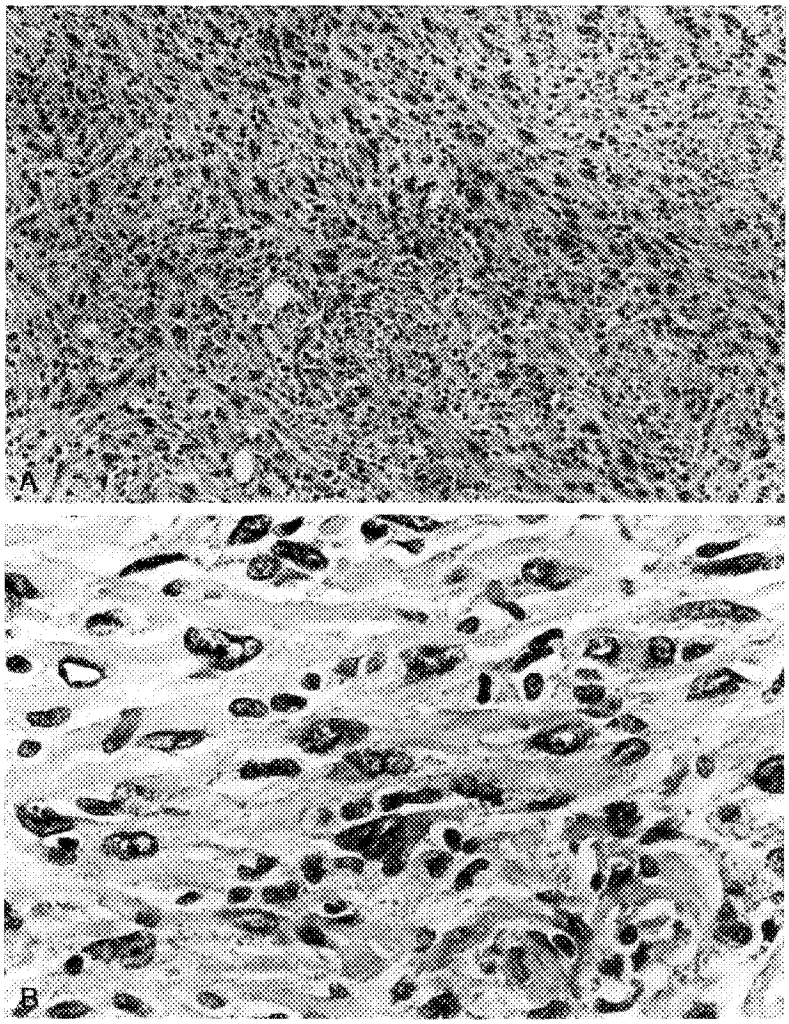

Figure 14. Photomicrographs of a malignant fibrous histiocytoma (MFH) of bone. *A*, At low magnification, a "storiform" pattern of interweaving bundles of tumor cells can be seen. *B*, At higher magnification, the prominent nuclear pleomorphism typical of an MFH is apparent. Mitoses are numerous, and there may be considerable tumor necrosis (not seen in this field). This tumor should be considered high grade by any classification.

complete response and did not go on to surgery. Three of the four patients who underwent surgery had complete responses, and one patient had a greater than 90 per cent tumor necrosis as determined by histologic examination of the resected tumor.

Enneking[24] speculated that adjuvant radiation therapy might be effective in suppressing residual disease. Capanna and associates[14] observed that of eight patients treated with radiation alone, three had cures and one had significant palliation.

In summary, the treatment of malignant fibrous histiocytoma of bone should include pre- and postoperative chemotherapy and at least wide surgical margins achieved by en bloc resection or amputation. Radiation therapy may be effective for residual disease or tumors in surgically inaccessible locations.

REFERENCES

1. Albright F, Butler AM, Hampton AO, et al: Syndrome characterized by osteitis fibrosa disseminata, areas of pigmentation and endocrine dysfunction, with precocious puberty in females. Report of five cases. N Engl J Med 216:727, 1937
2. Bacci G, Springfield D, Capanna R, et al: Adjuvant chemotherapy for malignant fibrous histiocytoma in the femur and tibia. J Bone Joint Surg 67A:620, 1985
3. Bertoni F, Calderoni P, Bacchini P, et al: Desmoplastic fibroma of bone. A report of six cases. J Bone Joint Surg 66B:265–268, 1984
4. Bertoni F, Capanna R, Calderoni P, et al: Case report 223. Benign fibrous histiocytoma. Skeletal Radiol 9:215–217, 1983
5. Bertoni F, Capanna R, Calderoni P, et al: Primary central (medullary) fibrosarcoma of bone. Semin Diagn Pathol 1:185–198, 1984
6. Blau RA, Zwick DL, Westphal RA: Multiple non-ossifying fibromas. A case report. J Bone Joint Surg 70A:299–304, 1988
7. Boland PJ, Huvos AG: Malignant fibrous histiocytoma of bone. Clin Orthop 204:130, 1986
8. Bosch AL, Olaya AP, Fernandez AL: Non-ossifying fibroma of bone. A histiochemical and ultrastructural characterization. Virchows Arch [Pathol Anat] 362:13–21, 1974
9. Brower AC, Culver JE Jr, Keats TE: Histological nature of the cortical irregularity of the medial posterior distal femoral metaphysis in children. Radiology 99:389, 1971
10. Caffey J: On fibrous defects in cortical walls of growing tubular bones. *In* Levine SZ (ed): Advances in Pediatrics, vol. 7. Chicago, Year Book Publishers, 1955, pp 13–51
11. Campanacci M, Laus M, Boriani S: Multiple non-ossifying fibromata with extraskeletal anomalies: A new syndrome? J Bone Joint Surg 65B:627–632, 1983
12. Campanacci M, Laus M: Osteofibrous dysplasia of the tibia and fibula. J Bone Joint Surg 63A:367–375, 1981
13. Campbell CJ, Hawk T: A variant of fibrous dysplasia (osteofibrous dysplasia). J Bone Joint Surg 64A:231–236, 1982
14. Capanna R, Bertoni F, Bacchini P, et al: Malignant fibrous histiocytoma of bone. Cancer 54:177–187, 1984
15. Clarke BE, Xipell JM, Thomas DP: Benign fibrous histiocytoma of bone. Am J Surg Pathol 9:806–815, 1985
16. Cline MJ, Golde DW: A review and reevaluation of the histiocytic disorders. Am J Med 55:49–60, 1973
17. Dahlin DC: Bone Tumors: General Aspects and Data on 6221 Cases, ed 3. Springfield, IL, Charles C Thomas Co, 1978
18. Dahlin DC: Infantile fibrosarcoma (congenital fibrosarcoma-like fibromatosis). Skeletal Radiol 8:77–78, 1982
19. Dahlin DC, Unni KK, Matsuno T: Malignant (fibrous) histiocytoma of bone—fact or fancy? Cancer 39:1608–1616, 1977
20. den Heeten GJ, Koops HS, Kamps WA, et al: Treatment of malignant fibrous histiocytoma of bone. A plea for primary chemotherapy. Cancer 56:37, 1985
21. Destouet J, Kyriakos M, Gilula L: Fibrous histiocytoma (fibroxanthoma) of a cervical vertebra. Skeletal Radiol 5:241–246, 1980
22. Dorfman HD: Malignant transformation of benign bone lesions. Proc Seventh Nat Cancer Conf, American Cancer Society, 1973, pp 901–913
23. Enneking WF, Gearen PF: Fibrous dysplasia of the femoral neck. Treatment by cortical bone-grafting. J Bone Joint Surg 68A:1415–1422, 1986
24. Enneking WF: Musculoskeletal Tumor Surgery. New York, Churchill Livingstone, 1983
25. Fechner RE, Spjut HJ, Haggitt RC: Diseases of Bones and Joints. Proc 51st Am Soc Clin Pathol, Chicago, ASCP Press, 1985, pp 12–17
26. Frangenheim P: Angeborene osteitis fibrosa ala ursache einer intrauterine unterschenkelfraktur. Arch Klin Chir 117:22–29, 1921
27. Freeman BH, Bray EW, Meyer LC: Multiple osteotomies with Zickel nail fixation for polyostotic fibrous dysplasia involving the proximal part of the femur. J Bone Joint Surg 69A:691, 1987
28. Gephardt MC, Campbell CJ, Schiller AL, et al: Desmoplastic fibroma of bone. A report of eight cases and review of the literature. J Bone Joint Surg 67A:732–747, 1985
29. Greyson ND, Pang S: The variable bone scan appearances of nonosteogenic fibroma of bone. Clin Nucl Med 6:242, 1982
30. Groopman JE, Goldi DW: The histiocytic disorders: A pathophysiologic analysis. Ann Intern Med 94:95–107, 1981
31. Harris WH, Dudley HR, Barry RJ: The natural history of fibrous dysplasia. J Bone Joint Surg 44A:207–233, 1962
32. Hatcher CH: The pathogenesis of localized fibrous lesions in the metaphyses of long bones. Ann Surg 122:1016, 1945
33. Herrera GA, Reimann BEF, Scully TJ, et al: Nonossifying fibroma. Electron microscopic examination of two cases supporting a histiocytic rather than a fibroblastic origin. Clin Orthop Rel Res 167:269, 1982
34. Hunter D, Turnbull HM: Hyperparathyroidism: Generalized osteitis fibrosa. With observations upon the bones, the parathyroid tumors, and normal parathyroid glands. Br J Surg 19:203, 1931

35. Huvos AG, Heilweil M, Bretsky SS: The pathology of malignant fibrous histiocytoma of bone. Am J Surg Pathol 9:853–871, 1985
36. Huvos AG, Higinbotham NL, Miller TR: Bone sarcomas arising in fibrous dysplasia. J Bone Joint Surg 54A:1047–1056, 1972
37. Huvos AG, Higinbotham NL: Primary fibrosarcoma of bone. A clinicopathologic study of 130 patients. Cancer 35:837–847, 1975
38. Jaffe HL: Fibrous cortical defect and non-ossifying fibroma. *In* Tumors and Tumorous Conditions of the Bones and Joints. Philadelphia, Lea & Febiger, 1958, pp 76–96, 243
39. Jaffe HL: Fibrous dysplasia. *In* Tumors and Tumorous Conditions of the Bones and Joints. Philadelphia, Lea & Febiger, 1958, pp 117–141
40. Jaffe HL, Lichtenstein L: Non-osteogenic fibroma of bone. Am J Pathol 18:205, 1942
41. Johnson LC: Congenital pseudarthrosis, adamantinoma of long bone and intracortical fibrous dysplasia of the tibia. J Bone Joint Surg 54A:1355, 1972
42. Kempson RL: Ossifying fibroma of the long bones. Arch Pathol 82:218–233, 1966
43. Kimmelstiel P, Rapp I: Cortical defect due to periosteal desmoids. Bull Hosp Joint Dis 12:286–287, 1951
44. Lagace R, Delage C, Bouchard HL, et al: Desmoplastic fibroma of bone. An ultrastructural study. Am J Surg Pathol 3:423–430, 1979
45. Larsson S, Lorentzon R, Boquist L: Fibrosarcoma of bone. A demographic, clinical and histopathological study of all cases recorded in the Swedish cancer registry from 1958–1968. J Bone Joint Surg 58B:412–417, 1976
46. Lazarus SS, Trombetta LD: Non-ossifying fibroma or benign lipoblastoma of bone—an electron microscopic and histochemical study. Histopathology 6:793–805, 1982
47. Lichtenstein L: Bone Tumors. St. Louis CV Mosby Co, 1977, pp 112–126
48. Lichtenstein L, Jaffe HL: Fibrous dysplasia of bone. A condition affecting one, several or many bones, the graver cases of which may present abnormal pigmentation of skin, premature sexual development, hyperthyroidism or still other extraskeletal abnormalities. Arch Pathol 33:777, 1942
49. Markel SF: Ossifying fibroma of long bone: Its distinction from fibrous dysplasia and its association with adamantinoma of long bone. Am J Clin Pathol 69:91–97, 1978
50. McCarthy EF, Matsuno T, Dorfman HD: Malignant fibrous histiocytoma of bone: A study of 35 cases. Hum Pathol 10:57–70, 1979
51. McCune DJ, Bruch H: Osteodystrophia fibrosa. Report of a case in which the condition was combined with precocious puberty, pathologic pigmentation of the skin and hyperthyroidism, with a review of the literature. Am J Dis Child 54:806, 1937
52. Miller RL, Sheeler LR, Bauer TW, et al: Erdheim-Chester disease. Case report and review of the literature. Am J Med 80:1230–1236, 1980
53. Mirra JM: Bone Tumors. Diagnosis and Treatment. Philadelphia, JB Lippincott, 1980
54. Mirra JM, Gold RH, Rand F: Disseminated nonossifying fibromas in association with café-au-lait spots (Jaffe-Campanacci syndrome). Clin Orthop Rel Res 168:192, 1982
55. Montgomery AH: Ossifying fibromas of the jaw. Arch Surg 15:30, 1927
56. Nakashima Y, Yamamuro T, Fujiwara Y, et al: Osteofibrous dysplasia (ossifying fibroma of long bones). A study of 12 cases. Cancer 52:909–914, 1983
57. Pennes DR, Braunstein EM, Glazer GM: Computed tomography of cortical desmoid. Skeletal Radiol 12:40, 1984
58. Resnick D, Greenway G: Distal femoral cortical defects, irregularities and excavations. A critical review of the literature with the addition of histologic and paleopathologic data. Radiology 143:345, 1982
59. Resnick D, Niwayama G: Diagnosis of Bone and Joint Disorders. Philadelphia, WB Saunders, 1988
60. Roessner A, Immenkamp M, Wiedner A, et al: Benign fibrous histiocytomas of bone: Light and electron microscopic observation. J Cancer Res Clin Oncol 101:191–199, 1981
61. Savage PE, Stoker DJ: Fibrous dysplasia of the femoral neck. Skel Radiol 11:119–123, 1984
62. Schajowicz F: Tumors and Tumorlike Lesions of Bone and Joints. New York, Springer-Verlag, 1981
63. Schoenecker PL, Swanson K, Sheridan JJ: Ossifying fibroma of the tibia. J Bone Joint Surg 63A:483–488, 1981
64. Sim FH, Wold LE, Swee RG: Fibrous Tumors of Bone. Part II. AAOS Instructional Course Lectures, vol 33. 1984, pp 40–59
65. Sontag LW, Pyle SI: The appearance and nature of cyst-like areas in the distal femoral metaphysis of children. Am J Roentgenol 46:185, 1941
66. Spanier SS, Enneking WF, Enriquez P: Primary malignant fibrous histiocytoma of bone. Cancer 36:2084–2098, 1975
67. Spjut HJ, Fechner RE, Ackerman LV: Tumors of bone and cartilage [suppl]. *In* Atlas of Tumor Pathology, 2nd ser., fasc. 5. Washington, DC, Armed Forces Institute of Pathology, 1981
68. Steiner GC: Fibrous cortical defect and nonossifying fibroma of bone. Arch Pathol 97:205–210, 1974
69. Stephenson RB, London MD, Hankin FM, et al: Fibrous dysplasia. An analysis of options for treatment. J Bone Joint Surg 69A:400–409, 1987
70. Taconis WK, Van Rijssel TG: Fibrosarcoma of long bones. A study of the significance of areas of malignant fibrous histiocytoma. J Bone Joint Surg 67B:111–116, 1985
71. Urban C, Rosen G, Huvos AG, et al: Chemotherapy of malignant fibrous histiocytoma of bone. A report of five cases. Cancer 51:795, 1983
72. Von Recklinghausen F: Die fibrose oder deformiende Osteite. Berlin, Festschrift Rudolf Virchow zu seinem 71 Geburtstage, 1891
73. Weiner M, Sedlis M, Johnston AD, et al: Adjuvant chemotherapy of malignant fibrous histiocytoma of bone. Cancer 51:25, 1983
74. Young JWR, Levine AM, Dorfman HD: Case Report #293. Nonossifying fibroma of the upper tibial diametaphysis with considerable increase in size over a three year period. Skeletal Radiol 2:294–297, 1984

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